TUBO-OVARIAN ABSCESS: PATHOGENESIS AND MANAGEMENT

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That a female patient with abdominal pain is often considered to have pelvic inflammatory disease until proven otherwise is ubiquitous in the medical literature. This view is dangerous and should be challenged because it has resulted in episodes of ruptured appendix, death from ruptured ectopic pregnancies, and serious morbidity from delayed diagnoses of such entities as diverticulitis and endometriosis. Proper diagnostic steps should be taken for all patients with abdominal pain of unclear etiology.

This article reviews the pathogenesis of tubo-ovarian abscesses so as to separate and clearly identify fact from fiction. Diagnostic steps and management guidelines are discussed.

Tubo-ovarian abscesses (TOAs) are serious complications of female upper genital tract infections, most commonly following exposure to sexually transmitted diseases (STDs). Tubo-ovarian abscesses frequently result in irreversible tubal and ovarian damage, and therefore pose a serious threat to fertility. They may also be accompanied by other complications,[1,2] such as incapacitating pelvic pain, ectopic pregnancy,[3] abscess rupture,[4] and bowel obstruction.

In the overwhelming majority of cases, TOAs are sequelae of salpingitis.[1,2,5] As with salpingitis they are found predominantly in sexually active women of low parity who have been exposed to STDs,[6] multiple partners,[7] or to partners with multiple sexual partners,[7,8] regardless of race, marital status, or contraceptive choice. An important step in the prevention of TOAs is the prevention of salpingitis. If salpingitis is suspected, prompt diagnosis[9-11] and proper treatment[1,5,10-12] are the next best strategy for prevention of TOA formation.

RISK FACTORS

The most important risk factor in the pathogenesis of TOAs is sexual activity with an infected partner. There are frequently clues in the history, physical examination, or laboratory results that suggest the possibility of exposure to microorganisms capable of initiating tubal inflammation (Tables 1 and 2).

Multiple Sexual Partners

Exposure to sexually transmitted pathogens capable of causing tubal infection is most likely in premarital or extramarital sexual encounters by either partner. Knowledge about a history of geni-

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TABLE 1. HISTORY AND LABORATORY FINDINGS THAT REQUIRE FURTHER INVESTIGATION TO RULE OUT EXPOSURE TO SEXUALLY TRANSMITTED DISEASES

Multiple sexual partners
History of vaginitis, cervicitis, endometritis or salpingitis
Occurrence of previous sexually transmitted diseases (STDs)—Bartholin abscess
Partner with history of STDs
Partner with history of nongonoccocal urethritis or postgonoccocal urethritis
Unexplained pyuria or dysuria
Papanicolaou smears with report of inflammation
Unexplained infertility
Unexplained episodes of pelvic or abdominal pain
Unexplained episodes of menstrual irregularity
Unexplained treatment with antibiotics
Unexplained pharyngitis
History of right upper quadrant pain with normal liver function tests
History of unexplained fever

tal infection in a new partner is less likely early in a sexual relationship. Ideally, a previously sexually active person would undergo an examination prior to sexual activity with a new partner and a follow-up examination within a month of exposure to the new partner. This screening would presumably include urinalysis, Papanicolaou smear, and serologic tests for Chlamydia,[13] syphilis,[14] and acquired immune deficiency syndrome (AIDS),[15] microscopic examination of genital secretions for detection of sexually transmitted organisms and Mobiluncus[16] as well as culture for Mollicutes,[17] Neisseria gonorrhoeae,[18] Chlamydia,[18,19] and herpes.[19] A thorough history would indicate whether the oropharynx or anal canal required additional screening for sexually transmitted diseases.[20–22] The presence of mucopurulent cervicitis,[23] unexplained inflammation on the Papanicolaou smear,[24] nongonoccocal urethritis (NGU),[25,26] pyuria,[26–31] or positive serology[13,32] would be followed up with appropriate diagnostic studies to rule out the presence of sexually transmissible pathogens. The presence of genital lesions,[33] skin lesions,[33–35] or adenopathy[36] would be followed by a thorough evaluation to establish etiology and to administer appropriate therapy.

Unfortunately, first sexual encounters are frequently of a nature that precludes a rational approach to disease prevention, and as a consequence, an ideal screen is seldom, if ever, performed before the fact.

Pyuria

The presence of pyuria in a sexually active woman requires screening for Chlamydia trachomatis,[25,30,31] particularly if none of the common bacteria associated with urinary tract infections can be recovered from the urine.[26] Occasionally urethritis may be caused by Neisseria gonorrhoeae,[28] Trichomonas vaginalis and Candida albicans.[29] However, Candida urethritis does not usually cause pyuria.[29]

Sexually active women with clinical symptoms of cystitis must undergo a screen for pathogens that includes sexually transmitted organisms by the use of special techniques that selectively favor the detection of Chlamydia trachomatis and Neisseria gonorrhoeae. This is especially true if they do not fulfill the traditional criterion of more than 100,000 coliforms per milliliter[37] and they also have pyuria. The presence of signs and symptoms suggestive of lower urinary tract bacterial infection in sexually active women should prompt physicians to distinguish patients with a sexually transmitted disease from those with otherwise uncomplicated urinary tract infections at the time of the initial visit. Failure to recognize the presence of C trachomatis or N gonorrhoeae in susceptible women with urinary signs and symptoms due to infection with these organisms allows these pathogens to establish an infection in the upper genital tract with subsequent development of salpingitis and eventually TOA.

Vaginitis/Vaginosis

Vaginitis is probably the most common disease seen by gynecologists in general practice.[38-40] Most of these patients will have vaginal symptoms of discharge, offensive odor, pruritus, soreness, or a combination of these symptoms. Culture or microscopy reveals Candida, Trichomonas, Gardnerella, Mobiluncus,[16] Mollicutes,[17,38] or

mixed bacterial flora.[16,39,40] With the exception of Candida, infection with any of these agents suggests exposure to the genital flora of multiple persons by at least one of the sexual partners. Proper management of vaginitis[39-40] or vaginosis[16] in sexually active women requires the identification of causative agents. This investigation is best done at the initial visit prior to therapy. The detection of "clue cells,"[16,38] Gardnerella vaginalis,[38,39] Trichomonas vaginalis,[38] or Mollicutes[17,38] may signal the presence of other pathogens. Identification of a sexually transmitted organism enhances the probability of recovery of other sexually transmitted pathogens, including the ones associated with salpingitis and TOA, such as Chlamydia trachomatis, Mollicutes, or gonococci.

TABLE 2. PHYSICAL FINDINGS THAT REQUIRE INVESTIGATION TO RULE OUT EXPOSURE TO SEXUALLY TRANSMITTED DISEASES

Mucopurulent cervicitis
Tenderness on abdominal or pelvic examination
Vaginal discharge
Urethral discharge
Abnormal pelvic mass
Genital lesions (blisters, ulcers, warts)
Arthritis, dermatitis
Ophthalmitis, conjunctivitis
Lymphadenopathy
Laparoscopy—Laparotomy scar for unknown reasons
Fever of unknown origin

Cervicitis

The infected cervix is a reservoir for potential upper genital tract pathogens and for the sexual transmission of genital pathogens.[7] In the nonpregnant sexually active woman, cervicitis may lead to upper genital tract infection by sperm transport of pathogens[8,41,42] into the endometrial cavity, fallopian tube lumen, or peritoneal cavity during intercourse. An alteration of the tubal mucosa renders the fallopian tube vulnerable to invasion and damage by endogenous aerobic and anaerobic bacteria in susceptible hosts. If ovulation occurs at a time of active infection, the stroma of the ovary becomes exposed to the inflammatory process. When the challenge to the immune system is overwhelming enough to prevent local destruction of pathogens, an abscess develops as the host's next line of defense. If the woman happens to be ovulating at the time, the stroma of the ovary may become infected and a TOA may develop.

Other avenues of spread to the upper genital structures exist. Direct extension along mucosal surfaces[43,44] as well as hematogenous and lymphatic spread[45,46] are known alternate routes.

Mucopurulent cervicitis[23] is defined as an inflammation of the cervix with polymorphonuclear leukocytes present in the endocervix, demonstrated either by visible mucopus on a cotton-tip applicator or by the presence of ten or more leukocytes per oil immersion field on a Gram stain of endocervical mucus uncontaminated by vaginal discharge.

Chlamydia trachomatis has been isolated from 58 percent of women with mucopurulent cervicitis and from 5 percent of women without mucopurulent cervicitis.[47] Cervicitis may also be associated with gonococcal infection, especially if symptoms of acute upper genital tract infection are present simultaneously. Although the classical clinical presentation of chlamydial cervicitis may be silent, cervical inflammation and upper tract involvement may be severe.[9,23]

Herpes simplex virus produces ulcerative lesions on the vulva, vagina, and cervix.[38] It may also be a cause of ulcer production in the upper genital tract.[19] Herpes simplex virus has been recovered from the endocervix in the absence of vulvar, vaginal or ectocervical lesions.[38] In cases of herpes or gonococcal cervicitis, a mucopurulent exudate from the endocervix does not appear to occur as consistently as in cases where Chlamydia trachomatis is recovered.[19] Other aerobic and anaerobic bacteria have been recovered from the endocervix without evidence of an endocervical inflammatory response.[48]

It is clear that the cervix is an important microbial reservoir for infection of the upper genital tract and pelvis in sexually active women or in women undergoing gynecologic procedures.[49] There is evidence that inflammation with reparative atypia detected on Papanicolaou smears or in cervical biopsies may indicate chlamydial infection.[24] It is

then logical to test for the presence of Chlamydia trachomatis, Neisseria gonorrhoeae, and herpes in women with mucopurulent cervicitis or with evidence of inflammation on Papanicolaou smears, regardless of race, contraceptive choice, marital or socioeconomic status.

Endometritis

Endometritis in the nonpuerperal sexually active woman usually represents an intermediate infection stage between cervicitis and salpingitis.[50,51] The presence of more than 10 plasma cells per high power field in an endometrial specimen correlates well with chlamydial endometritis and cervicitis. If there is endometritis, Chlamydia trachomatis is more likely to be recovered from endometrial cultures than from endocervical cultures.[52] A negative culture for Chlamydia and gonorrhea from the cervix does not rule out the presence of these organisms in the genital tract. The main symptoms suggestive of endometritis are lower abdominal pain and intermenstrual spotting or bleeding. Laparoscopic examination of women with early signs of upper genital infection may not demonstrate visible fallopian tube inflammation even if there is microbiologic and serological evidence of chlamydial infection.[53] Serologic screening of sexually active women with early upper genital tract infection may be a more sensitive indicator of active chlamydial infection than culture or direct fluorescent antibody tests. The main disadvantage of chlamydial detection by identification of specific IgA and IgG is the inability to determine the exact site of infection in the genital tract. However, exact localization may be academic. It may be more important to identify consistently known fallopian tube pathogens when they are present, preferably prior to tubal damage.

Salpingitis

Salpingitis is an inflammation of the fallopian tubes that usually results from an infection with sexually transmitted pathogens in susceptible nonpregnant women.[2,18,53-61] The probability of acquiring salpingitis is directly proportional to the number of sexual partners[54,60,62,63] or to the number of sexual partners to whom the male consort has been exposed.[42] Inflammation is most likely a response to an initial infection with certain immunotypes (D-K) of Chlamydia trachomatis,[53,59] Neisseria gonorrhoeae,[18,23,27,54,59] Mollicutes,[17,32,59] and possibly ulcer-producing organisms such as herpes simplex virus.[19] Although aerobes and anaerobes that constitute part of the endogenous lower genital tract flora[48] have been recovered from infected fallopian tubes,[2,4,5,64,65] it is unlikely that these organisms initiate an inflammatory response in healthy fallopian tubes. These organisms have been recovered from the endometrium and peritoneal cavity in the course of experimental observations with no evidence of disease by clinical signs, direct visualization of pelvic organs, or by histologic examination of the endometrium.[66-68] Recovery of these organisms from the fallopian tubes at the time of an established inflammatory process[55,64,65] does not necessarily identify them as the pathogens that initiated the process. It is likely that in salpingitis, endogenous organisms invade the fallopian tubes following an initial infection with organisms such as Neisseria gonorrhoeae or Chlamydia trachomatis, which are known to initiate inflammation and damage to the tubal mucosa and fimbriae.[18,19,69-71]

Destruction of the basement membrane of the fallopian tubal mucosa has been demonstrated in the laboratory following exposure to E coli endotoxin.[72] This event prevents regeneration of cilia destroyed by adherence, fracture, and lysis following an antecedent inflammatory response to an infectious process. Under normal conditions it is unlikely that endotoxin alone is capable of initiating tubal damage. This event has not been associated with treatment of women for infections elsewhere in the body, even when antibiotics effective against E coli or other organisms with endotoxin are used. Neither is tubal damage a complication in women treated for endotoxic shock. Chlamydial and gonococcal inflammation of the fallopian tubes are known to be associated with an initial stage of fimbrial conglutination and adhesion formation in the villi during an active infection.[18,19,69-73] Hyperplasia of the visceral peritoneum of the distal end of the tube causes phimosis and eventual inversion of the fimbriae with formation of the classical "clubbed tube." Prevention of superinfection with coliforms and

anaerobes early in the disease process may prevent destruction of the basal layer by endotoxin.

Determination of pelvic inflammatory disease causation by endogenous organisms can be made only after absence of prior exposure to exogenous tubal pathogens is demonstrated by appropriate microbiological and serological studies. To establish causation, such studies must also demonstrate that the untreated sexual partners of the patient do not harbor known tubal pathogens. In short, if under normal conditions anaerobes cause upper genital infection, the occurrence of salpingitis in strictly monogamous couples who are otherwise healthy must be demonstrated in the absence of prior pelvic or abdominal surgical procedures.

Sperm may be an important vehicle for the transport of upper genital tract pathogens such as Chlamydia trachomatis[41,42,74-78] and Neisseria gonorrhoeae[79-82] to the fallopian tubes. Bacteria,[77] including sexually transmitted pathogens,[41,78-82] have been shown to attach to sperm. It has also been shown that female partners of infected men with motile sperm in the ejaculate have a significantly higher incidence of upper genital tract infection than partners of infected men who have had a vasectomy.[42]

The number of male sexual partners and frequency of intercourse with an infected male partner also may have an effect in addition to the obvious one of repeated exposure. Seminal fluid contains an inhibitor of complement activation,[82] which may protect tubal pathogens from the hosts antibodies. The probability of infection may be directly related to the degree of complement inhibition.

Bacteria can also gain access to the upper genital tract by mucosal spread,[43-46] menstrual flow,[83] blood vessels,[45,46] lymphatic channels,[45,46] and possibly by attachment to, or ingestion by, Trichomonas vaginalis.[84]

Salpingitis is the most common disease predisposing to the development of tubo-ovarian abscesses. Although symptoms of salpingitis are most common around the time of menstruation, clinical manifestations can occur at any time of the menstrual cycle. Explanations based on the presence of menstrual blood,[83] the role of the cervical mucus,[55,68,83] and the effects of socioeconomic and racial factors,[55,83] although interesting, are speculative and not established so far by well-controlled studies. It is more likely that the development of symptoms is the result of a combination of the properties of the infecting organisms[18,85] and the immune response of the host[86] at an opportune time in the disease process. The critical balance may be altered more frequently at the time of menses as far as the development of symptoms is concerned, but menstruation is not an indispensable event for the development of salpingitis.

Intrauterine Devices, Age, Socioeconomic and Racial Factors

There are conflicting reports on the effect of intrauterine devices (IUDs) on the pathogenesis of pelvic inflammatory disease (PID) and tubo-ovarian abscess.[62,87-104] Conflicting conclusions have resulted even from analysis of the same data.[62,95,98] Burkman[62] found no difference in the incidence of PID requiring hospitalization in black women whether or not they used IUDs. He found no significant difference either between IUD types and the rate of hospitalization for PID. Lee et al[95] found striking differences in the rate of hospitalization for PID according to the IUD type by reanalysis of the same data following ex post facto modification of the criteria for admission to the study. In neither of the reports[62,95] were the criteria for hospitalization spelled out. Although the data reported thus far indicate that among hospitalized patients with a diagnosis of PID there is likely to be an overrepresentation of women with IUDs,[62,95,96] there is little evidence to indicate that women with IUDs develop PID at a higher rate than women without IUDs if sexual experience is taken into account. Most of the published reports do not correct for the possibility that IUDs were initially inserted preferentially in women at high risk for PID[105,106]: young, single, sexually active women from unstable homes, or unreliable and poorly motivated women[105] who are likely to have multiple partners.[106]

Most of the studies linking PID to IUD use have been done in hospitalized patients. There are several factors that influence the decision of whether to hospitalize a woman suspected of having PID.[107] Among them, socioeconomic status, marital status, type of hospital, and whether the

woman uses an IUD.[62,103] Retrospective studies in hospitalized patients cannot establish a cause-and-effect relationship. In a retrospective study of the correlation of PID and IUD use in hospitalized patients, there is usually a strong Berkson bias,[108] in addition to other sampling and measurement biases difficult to control in retrospective studies,[108] that makes an establishment of causation impossible. The difficulty in making an accurate diagnosis of PID on clinical findings has been well established.[10,109-111] It is also well known that a decision to hospitalize women with PID in the United States is dependent not only on a clinical impression of PID.[107] Therefore, conclusions based on hospitalized patients[62,95,96] without uniform confirmation of the diagnosis by objective criteria[10,109-111] cannot be accepted as definitive, and the association of these findings with specific contraceptives[95,96] are, at best, tenuous. Terms like "risk of development of PID" and "risk of hospitalization for PID" are at times used interchangeably.[95] There is no evidence that these are equivalent events. These two events may in fact be unrelated, particularly if there are no established criteria for hospitalization.

The relationship between salpingitis and cervicitis[23,47] and the observation that trichomonas can ascend into the fallopian tubes,[84] as well as the demonstration of bacterial attachment to sperm,[41,42,74-82] argues against the hypothesis that in sexually active women the endometrial cavity is normally sterile.[66-68] These observations suggest that the endometrial flora may be directly related to the frequency of intercourse, to the genital flora of the partners, to the number of sexual partners, and to the presence or absence of vaginitis or cervicitis.

Even if the hypothesis that endometrial colonization by capillary action along IUD tails[66,68] is shown to occur in some instances (and this event has not been demonstrated unequivocally in humans), the significance of this phenomenon in sexually active women is likely to be of little or no consequence. Bacteria have ready access to the upper genital tract via sperm and along the moist mucosal surfaces of the vagina, cervix, uterine cavity, and fallopian tubes. Organisms normally found in the vagina have reportedly been recovered from the cul-de-sac of healthy women not using IUDs.[112] It is likely that prior exposure to pathogens that cause mucosal damage is a prerequisite for tubal infection with endogenous bacteria. Mucosal pathogens such as Chlamydia trachomatis and Neisseria gonorrhoeae have special growth requirements that would make survival along or within the tail of an IUD extremely difficult.

Few studies on the epidemiology of salpingitis have fully corrected for the limitations imposed by retrospective analysis conducted on hospitalized patients or patients attending subspecialty clinics. Results based on data collected from hospitalized patients[95,96,113] or from patients attending subspecialty clinics[63,114] that link IUD use and PID, without a definition of the criteria for admission to the hospital or clinic, should be taken with extreme caution, and may not be accepted as conclusive until a well-controlled, prospective, blinded study supports such conclusions.

Cohort[91,94,101] and prospective randomized studies[90] have failed to demonstrate significant differences in PID prevalence or incidence between patients using different IUDs. A comparison between women using contraception and sexually active women matched for sexual experience but using no contraception is lacking in most studies. There are at least two problems with controls using other forms of contraception: some contraceptives may protect some patients from developing salpingitis,[62,63,73] and the effectiveness of protection between the different forms may be unequal.[73,115]

The problems with studies attempting to compare tubal infertility with contraceptive choice[63,114] are formidable. In addition to the inherent problems that exist with a retrospective assessment of tubal infertility in a nonrandomized numerator of women with an antecedent history of IUD use, there is no knowledge about the denominator from which the numerator derives. Furthermore, the percentage of sexually active women with tubal infertility in the general population is not known. Publicity and litigation involving contraceptive methods at the time the studies are done are likely to influence the proportion of patients seeking evaluation for tubal infertility in an uneven way for different contraceptives. If the controls are women using barrier and hormonal contracep-

tives, there is likely to be a double effect of different degrees of protection from PID in women using contraceptives other than IUDs,[73,111] and an increased proportion of infertile women who used IUDs as a form of contraception seeking evaluation for litigation purposes. Both of these effects are in the same direction, and may not be equal for all IUDs. Knowledge about numerators and denominators as well as life history of sexually transmitted diseases, sexual partners, and of gynecologic surgical procedures are essential to assess the role of IUDs in tubal infertility, salpingitis, and tubo-ovarian abscess. The impression that a causal relation between IUDs and PID is demonstrated[116] on the basis of results from studies not controlled for these important confounding variables is erroneous.

The need for careful controls and knowledge of incidence and prevalence of an event in the general population is underscored by the initial associations of Actinomyces with IUDs[117] and the failure to demonstrate such an association with controlled studies done prospectively.[118-120] A similar experience resulted with the association of unilateral tubo-ovarian abscess with IUDs.[121-123] The early reports suggested that unilateral abscesses were a unique entity associated with IUDs.[121,122] Subsequent reports indicated that unilateral TOAs could develop in the absence of a history of IUD use,[123,124] and later studies concluded that there was little difference, if any, in the incidence of unilateral TOAs between IUD users and nonusers.[1,5,115,125,126] Studies that report an association between IUDs, tubal infertility, PID, and TOAs have failed to control for all variables known to strongly influence the incidence of PID, such as history of infection with relevant sexually transmitted pathogens,[6-9,127,128] the presence of cervicitis,[23,47] sexual lifestyle,[106,129] and the objective establishment of the diagnosis of PID in all participating patients.[10,11,109-111] Until a randomized well-controlled study that follows strict preestablished guidelines is performed, extreme caution must be exercised in the interpretation of results obtained by retrospective analysis of selected patients for whom a diagnosis of PID is not confirmed objectively and the criteria for admission into a specific group, hospital, or clinic is unknown.

The rate of complications with contraceptives, including so-called IUD-related infections, may be directly related to the experience and knowledge of the inserter. IUD insertion in sexually active women must take place only after the presence of genital infection is ruled out. Failure to detect the presence of potential tubo-ovarian pathogens or signs of subclinical urogenital infection endangers a woman's reproductive future whether or not she chooses an IUD as a contraceptive. As late as the 1980s, many clinicians who inserted IUDs were not aware of the prevalence, incidence, or potential for reproductive damage of Chlamydia trachomatis. Screening for Neisseria gonorrhoeae was frequently ignored by others.The presence of STDs is closely related to sexual lifestyle.[106,129] Therefore, the effect of inadequate screening on subsequent pelvic infection when women are fitted with IUDs will be different for different individuals.[62]

For these reasons, it is not possible to compare accurately event rates of IUD performance with insertions performed at different times, in different populations, and with different personnel.[90] If adequate measures are not taken in study designs to eliminate the effects of all confounding variables, sophisticated mathematical and statistical analyses do not correct for sampling and measurement errors. The fact that clinical data are subjected to statistical analysis improves neither the accuracy of the results nor the validity of the conclusions.

Socioeconomic status, race,[55,62,113] and age[8] have not been shown to be risk factors for the development of PID independent of exposure to sexually transmitted diseases or to multiple partners. The age distribution of PID patients is identical with that of women with uncomplicated STDs.[7,8] Monogamous couples have not been shown to have different rates of genital infection, regardless of age, race, socioeconomic status, or contraceptive choice.[62,63] The prevalence of PID is directly related to sexual activity and to the number of sexual partners.[7-9,127-129]

The data relating PID to smoking,[114] age,[8,9] race, and socioeconomic status[2,55,64] are usually of the same qualitative nature of data used to describe an association between PID and IUD.[62,95,96] All of these variables are of questionable impor-

tance in the absence of strict controls for multiple sexual partners and sexually transmitted diseases. There is no evidence to suggest that age or race, for example, are the cause of PID, nor is there any evidence that a strict monogamous relationship between poor, nonwhite teenagers without sexually transmitted diseases carries a higher risk for PID. Smoking, age, socioeconomic and racial factors, although frequently cited,[62,114,130] have never been shown by properly controlled studies to be associated with salpingitis independent of exposure to multiple partners or to a single male partner who has had multiple partners. Demonstration that these are relevant variables as causative risk factors for PID is lacking. Socioeconomic factors are merely indicators of conditions that are likely to expose women to multiple partners or to partners with multiple partners. They do not in themselves have any other special predisposing effects for the development of salpingitis in the absence of exposure to sexually transmitted pathogens.

TUBO-OVARIAN ABSCESS FORMATION

An abscess is the result of the body's attempt to isolate an infectious process. Formed by encapsulation, an abscess is a collection of fluid containing a large number of aerobic and anaerobic bacteria with inflammatory cells and necrotic debris. The most common intraabdominal abscesses in women during the reproductive years are pelvic abscesses.

Tubo-ovarian abscesses are distinct entities, although frequently they are grouped with other pelvic abscesses in the literature.[1,5] Tubo-ovarian abscesses imply an extension of an inflammatory process from the fallopian tubes into the ovarian parenchyma with resultant suppuration. Tubo-ovarian abscesses are usually complications of sexually transmitted diseases, as is frequently the case with other more common pelvic abscesses.[1,5] In pelvic abscesses, the broad ligaments, adnexae, bowel, omentum, uterus, or pelvic wall (in any combination) may form the boundaries of an abscess cavity. Infectious complications of pregnancy[4,131] or gynecologic surgery,[131,132] malignancy,[105] and bowel perforation, including ruptured appendix[46,132] or diverticulum,[46,132] may be associated with pelvic abscesses. Ovarian abscesses are more commonly the result of disruption of the integrity of the capsule by ovulation or surgical trauma during a contaminated surgical procedure[133–135] or by bacterial stromal invasion via the hematogenous or lymphatic routes.[46,136]

Abscess formation is favored by compromise of the vascular supply to an area in close proximity to a mucosal surface that harbors several species of bacteria in its natural state.[85] Invasion of the tubal epithelium by mucosal pathogens initiates an inflammatory response that causes edema and pressure, which restricts the blood supply to the fallopian tubes. Leukocytes[137] defend against microbial invasion by secretion of substances that mobilize other components of the host's defense system and that facilitate phagocytosis. The lysosomal enzymes and resultant inflammatory reaction may, however, damage, to a certain extent, structures of the very host they are intended to protect. Endogenous organisms are normally in a symbiotic relationship with the host and are confined to specific areas in the body. Under normal conditions, the host's defense system controls the numbers and species of bacteria in areas of the gastrointestinal and genitourinary systems.[48,112] The vaginal and cervical bacteria, transported by spermatozoa or arriving to the fallopian tubes by mucosal extension, act in synergy with the exogenous microorganisms transmitted sexually to bring about an inflammatory reaction and eventual suppuration. In this complex microbial environment, organisms with structural or enzymatic factors[138,139] that favor their survival in susceptible hosts[140] will prevail.

Tubo-ovarian abscesses are usually found in sexually experienced, menstruating women who have been exposed to sexually transmitted diseases and who may have developed salpingitis in the absence of a contraceptive method that prevents ovulation. Tubo-ovarian abscesses reportedly occur in 3 to 16 percent of women with salpingitis[141,142] by the time they are admitted to a hospital. The initial clinical impression may be correct in only 30 percent of cases.[142] Tubo-ovarian abscesses reportedly constitute approximately 2 percent of gynecology admissions to urban hospitals.[143,144]

The certain diagnosis of TOA can be made only by direct observation during a surgical procedure, and confirmed by histologic evidence of an abscess involving the fallopian tube and ovary. Computerized tomography and ultrasonography[145–148] are useful to identify patients with clinical evidence of an inflammatory mass who may have an abscess from those who do not have an abscess, but they do not establish with certainty whether a cystic mass is a tubo-ovarian abscess.[148] Magnetic resonance imaging is an accurate localizing method that has the added advantage of providing information about anatomical and biochemical function, but there is little experience with this method in the diagnosis and management of TOAs.[149] Radionuclide[150] scanning is another promising diagnostic technique. Its accuracy in distinguishing abscesses from other cysts is reported to be excellent.

Patients with a pelvic abscess usually give a history of an insidious onset of symptoms that become progressively worse over a period of days or weeks, so that it is difficult to determine an exact date of onset. This is also the case with tubo-ovarian abscesses. The most consistent complaint is pelvic pain[5,142,145,151] and tenderness. Fever and tachycardia are frequently present, and some patients may complain of abnormal vaginal bleeding, vaginal discharge, nausea, anorexia, or diarrhea. On physical examination, lower abdominal and pelvic tenderness to palpation with or without rebound may be present. An abnormal mass is always present, but its clinical detection depends on location, the patient's weight, and the degree of tenderness to palpation. In difficult cases, sonography or computerized tomography are valuable adjuncts to the physical examination. False-positive results with sonography are extremely rare.[152,153] Computerized tomography has been reported to be the most accurate of the radiologic techniques evaluated for the localization of intraabdominal abscesses,[153] but it is an expensive method that at present is appropriate only when other noninvasive diagnostic procedures have failed to confirm the diagnosis.

Most patients with tubo-ovarian abscesses will have received antibiotics prior to a definite diagnosis. Some are given antibiotics at various times prior to hospitalization, which makes the bacteriologic assessment of an abscess difficult. Immunologic methods[13,32,65] may be useful for the identification of the organisms involved in the initiation and progression of the events that lead to abscess formation. Complex synergistic microbial relationships and host factors are interrelated in the pathogenesis of TOAs.[85,86,140,154] It is likely that even in cases of pelvic abscess, perhaps caused by a single or unusual organism,[155-158] there are other predisposing factors that are not detectable by the time the abscess is identified.

An abscess is an effective attempt by the host to contain an infection. Containment may be temporary or permanent, depending on host[140] and parasite[138,139] properties, and the direction in which the equilibrium is tilted following abscess formation. There is an interrelationship of complement with other host and microbial properties in the formation of an abscess, but there is evidence that the absence of thymic factors does not prevent containment by abscess formation.[85,86] Containment and control of bacterial proliferation has been found to be normal in the absence of thymic factors, though abscess size and neutrophil accumulation may be diminished.[86]

Management

Tubo-ovarian abscesses are part of the last line of defense against a sustained microbial challenge to the female reproductive system. With the formation of TOAs, the concern is primarily one of health and life preservation, and secondarily, reproductive potential. The preservation of reproductive integrity requires prevention of damage to the upper genital tract by avoiding exposure to sexually transmitted pathogens or by early intervention when there is a possibility of upper genital infection.

The reproductive potential will depend on how quickly the infectious process is contained and eliminated. The potential for severe or irreversible damage is greatest with involvement of the fallopian tubes and ovaries in the infectious process over an extended period of time that may be measured in days rather than weeks.

The success or failure of antimicrobial therapy alone will depend on the ability of the antibiotics selected to penetrate the abscess in effective con-

centration and on their ability to destroy bacteria and render them vulnerable in an abscess environment to natural host defenses.[159-162]

Adequate treatment of salpingitis is of importance in the prevention of tubo-ovarian abscess[11,12,163,164]; it includes establishing the diagnosis and extent of organ involvement early in the course of the disease,[10,11,164,165] detection of the organisms involved in the process including the initiating and superinfecting flora,[6,11,18,72,111] administration of appropriate antibiotics,[5,11,12,163,164] and follow-up of the patient and her partners. Salpingitis is a disease that requires hospitalization for definitive diagnosis and aggressive treatment. This approach is particularly important for patients suspected of having an early infection and who may be interested in preservation of fertility. Proper management is not complete without treatment of the sexual partners. An important source of recurrence is reexposure to an untreated or reinfected male partner who may be asymptomatic.

After adequate cultures, empiric treatment should be started with antibiotics effective against Neisseria gonorrhoeae, Chlamydia trachomatis, Mollicutes, and opportunistic endogenous aerobes and anaerobes. Early aggressive therapy directed against the initial pathogens may prevent the formation of tubal microdiverticula[43] and fimbrial adhesions.[44] If ovulation takes place during the initial stage of fimbrial inflammation, the probability of agglutination of the ipsilateral fimbriae to the ovulating ovary may be increased.

Following an initial episode of salpingitis, the patient should be started on oral contraceptives, unless there are contraindications for their use. Oral contraceptives may not protect effectively against salpingitis,[61] but they reduce the probability of progression to tubo-ovarian abscess formation by preventing exposure of the ovarian stroma to bacterial invasion from the tubal lumen as a byproduct of ovulation inhibition. The formation of a tubo-ovarian abscess follows migration of white blood cells[137] into the inflammatory complex with fluid accumulation as a transudate from tubal and ovarian tissue. Eventually a combination of inflammation and pressure necrosis leads to destruction of the tubo-ovarian wall or to abscess rupture with subsequent involvement of contiguous structures. The extent of damage will depend on the stage at which the chain of events leading to tubo-ovarian abscess rupture is interrupted. Rupture of the TOA is heralded by severe and sudden exacerbation of abdominal and pelvic pain, tachycardia out of proportion with the temperature, and signs of peritonitis and shock.

There is controversy as to whether patients with TOAs should have surgery shortly after initiation of antibiotic therapy or whether an attempt to achieve complete recovery by intense antibiotic therapy is appropriate.[5,125,131,132,151,166] It is suggested that surgical intervention should be reserved for cases where there is failure to respond to antibiotics after a predetermined period of treatment or where there is evidence of abscess rupture.[5,125,142]

There is agreement that once the diagnosis of pelvic abscess is entertained, steps to establish the diagnosis must be undertaken. If the diagnosis is confirmed or remains uncertain, the patient requires hospitalization and close observation.[5] Patients with tubo-ovarian abscess require parenteral antibiotics that are effective against anaerobic and aerobic bacteria known to be associated with pelvic abscesses.[1,11,12,141-144,151,167,168] The controversy revolves around the safety of managing a patient with an unruptured pelvic or tubo-ovarian abscess without surgical drainage.[1,5,11,151,166] The complex environment of an abscess frequently limits the effectiveness of antibiotics so that surgical intervention often becomes necessary.

There is also controversy regarding the extent of surgery in unilateral tubo-ovarian abscesses that require operative intervention because of a failure to respond to antibiotic therapy or because of rupture.[5] Unilateral adnexectomy with aggressive antibiotic therapy for women who desire to keep their reproductive potential does not seem to pose undue risks to patients who are followed closely after such an approach.[5,141] The risk of recurrence with this approach may be too high for a woman at the end of her reproductive years. The risk of rupture is ever-present with tubo-ovarian abscesses. This serious complication is associated with mortality even when properly managed.[4,105] It is unreasonable to expose a perimenopausal woman with an unruptured TOA to the risk of recurrence or rupture, unless there are other factors that

make surgery unreasonably dangerous. The extent of surgery has ranged from drainage by posterior colpotomy[131] to total abdominal hysterectomy and bilateral salpingal oopherectomy with removal of adjacent necrotic or inflamed tissue.[46,126] It is becoming apparent that the most appropriate approach to management of tubo-ovarian abscesses is individualized therapy that takes into account the age, clinical status, and desires of the properly informed patient.

SUMMARY

The best management of tubo-ovarian abscesses is prevention by identification of the woman at risk prior to the development of salpingitis and TOA.[8,168,169] Women with chlamydial antibodies are likely to have distal and peripheral fallopian tube disease.[110,168,169] These patients may be asymptomatic or exhibit minimal symptoms.[111] Mild disease requires prompt and aggressive treatment. Asymptomatic women with clinical or cytologic evidences of vaginitis,[38,39] cervicitis,[23,24] sterile pyuria, or the urethral syndrome[26-31] require a thorough screen for Chlamydia trachomatis, Neisseria gonorrhoeae, and herpes simplex in addition to other organisms associated with exposure to the genital flora of multiple individuals. The presence of any sexually transmitted pathogen should be followed by search and elimination of organisms known to initiate a series of events that culminate in the development of a TOA. Identification of sexually transmitted diseases must be followed by therapy involving the patient and her sexual partners, which should include information about epidemiology of STDs and complications that may result from recurrence or incomplete therapy. Reinfection or relapse is to be avoided by a suitable period of pelvic rest and a proper length of antibiotic coverage.

If a tubo-ovarian abscess is suspected, the patient must be admitted to the hospital and a protocol for management that assures the best outcome followed. A reasonable approach requires immediate surgery if noninvasive diagnostic tests and clinical evaluation suggest rupture of the abscess or an uncertain diagnosis. Tubo-ovarian abscesses in perimenopausal or postmenopausal women are best managed by immediate surgery following stabilization of the patient and adequate antibiotic coverage, unless there are compelling reasons not to use this approach.

Women in the reproductive years with an unruptured TOA may benefit from aggressive parenteral antibiotic coverage. Surgical intervention would then be reserved for cases where there is lack of response according to predetermined criteria. There must be sonographic evidence of abscess size reduction, absence of fever or leukocytosis, and reduction of pain within 48 hours. Abscess rupture during treatment would require immediate intervention. In the effective medical management of TOAs, time is of the essence, as resolution must take place prior to necrosis or irreversible damage by ischemia if reproductive function is to be preserved.

Medical management requires a thorough knowledge of antibiotic pharmacokinetics. Leukocytes mobilize to areas of bacterial invasion[137,170] and of decreased blood flow.[170] Therefore, antibiotics that concentrate in leukocytes and that retain effectiveness against relevant organisms in an abscess environment are the agents of choice.[171] Leukocyte delivery of antibiotics may facilitate bacterial destruction despite decreased blood flow and complex environmental conditions in abscesses, provided the antibiotic chosen is effective when there is an unusually large concentration of bacteria and are immune to destruction by the inoculum-size effect.[160] Antibiotics requiring active growth of organisms for efficacy may be less effective in an abscess environment.[159] The large number and multiple species of bacteria present may cause enzymatic inactivation of antibiotics[160] or transfer resistant plasmids to bacteria found to be sensitive in vitro.[162] Changes in the acidity and in the oxidation-reduction potential in an abscess may render certain powerful antibiotics ineffective,[161] while the concentration and activity of others may be enhanced.[171,172]

The only safe way to prevent tubo-ovarian abscess is to prevent salpingitis by avoiding exposure to sexually transmitted diseases. This is best achieved by a couple that establishes a monogamous relationship and abstains from casual or recreational sexual activity with multiple partners.

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